4

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,967	12/26/2001	Shigeru Kamei	087147-0443B	2213

22428 7590 06/27/2005

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,967	KAMEI ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *4-10 and 17-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 4/14/05, claims 1-3, 12-14 and 16 have been amended. Claims 4-10 and 17-25 remain withdrawn from consideration. Claims 1-3 and 11-16 are examined in this Office action.

Applicants' arguments filed 4/14/05 have been considered and found not persuasive.

✧

Claims 1-3 and 11-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,480,868. Although the conflicting claims are not identical, they are not patentably distinct from each other. Applicants have not traversed this rejection, so it is maintained without further comment.

✧

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have asserted that the compound of claim 16 is an LH-RH antagonist. However, there is no evidence that this is the case. Certainly, other antagonists of LH-RH are known. But the reality in pharmacology is that one cannot "predict" receptor antagonism or even receptor binding merely be viewing the structure of a compound. Minor changes in structure can result in elimination of activity. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

Given the unpredictability of structure/activity relationships, "undue experimenation" would be required of the skilled artisan to use the composition of claim 16 to antagonize LH-RH.

In response to the foregoing, applicants have argued that the examiner must have reason to doubt the particular species of claim 16 in order to maintain the rejection. However, this is not true. A finding of unpredictability can be justified without any proof that "failure" is inevitable. No court decision imposes such a high burden on an examiner. Nor does the examiner "single out" the particular compound of claim 16 as requiring "undue experimentation" to assess activity. The examiner asserts

that, as a general proposition, if one takes a compound which has been shown to antagonize LH-RH, and subsequently modifies the structure, "unpredictable" results are obtained with regard to the resulting propensity to antagonize LH-RH. Applicants are incorrect in arguing that the examiner is obligated to find a reference which discloses that someone tried to antagonize LH-RH using the compound of claim 16, and that the result was failure to antagonize.

The rejection is maintained.

✦

Claims 12-14 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 12 recites the phrase "about 5000 to about 25000", thus rendering the claim indefinite as to the upper and lower limits.

- Claim 13 recites the phrase "about 1.2 to about 4", thus rendering the claim indefinite as to the upper and lower limits.

- Claim 14 recites the phrase "about 0.01% to about 50%", thus rendering the claim indefinite as to the upper and lower limits.

  Applicants have argued that use of the term "about" has long been accepted practice in patent application prosecutions. The issue, however, is not simply that of the use of the term "about" in claims. Rather, the issue pertains to the use of the term "about" in reference to a range. Nor is the question that of whether some people find this to be "acceptable". There exist a number of laws in this society, the violation of which many people consider to be "acceptable". But once charged with a violation, the question of acceptability

becomes a secondary issue. With regard to the use of the term "about" in reference to a range, it remains the case that the claims are indefinite. For example, in the case of the range "about 1.2 to about 4", where would applicants draw the line between a lower limit that falls within the scope of the claim, and a lower limit that falls outside the scope of the claim? If applicants are unable to make this determination, then how can the skilled artisan?

✧

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 and 11 are rejected under 35 U.S.C. §102(e) as being anticipated by Haviv (USP 5,110,904).

Haviv discloses (cols 12-25) various peptides falling within the scope of instant claim 1. Also disclosed (col 27, line 8+) is that the peptide can be combined with a PLA/PLG copolymer.

Applicants have argued that since Haviv discloses some embodiments that fall outside the scope of the claimed invention in addition to those that fall within the scope of the invention, therefor the rejection is improper. However, the examiner disagrees. Applicants have also argued that they have reason to believe that Haviv deliberately selected conditions such that the terminal carboxyl groups formed in the PLA/PLG copolymer were converted by Haviv to some other functional group which applicants have declined to disclose. However, there is no evidence to support applicants speculation regarding the PLA/PLG copolymer referred to in the reference.

The rejection is maintained.

✧

The following is a quotation of 35 U.S.C. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-3 and 11-15 are rejected under 35 U.S.C. §103 as being unpatentable over Haviv (USP 5,110,904) in view of Boswell (USP 3,773,919).

The teachings of Haviv are indicated above. Boswell discloses various PLA/PLG polymers for use in pharmaceutical compositions. Boswell does not disclose any of the LH-RH antagonists to which the instant claims are drawn.

Applicants have argued that Haviv does not suggest the desirability of selecting compositions that contain PLA/PLG polymers together with a peptide that falls within the scope of the claimed invention. However, applicants are not correct. Haviv suggests (col 27, line 8+) the desirability of using the PLA/PLG polymers of Boswell patent.

It appears that the centerpiece of applicants' argument is to focus on the following statement which is provided on page 58, line 31-35 of the specification:

> "As shown in Comparative Examples 1 to 3, with a lactic acid-glycolic acid copolymer having substantially no terminal carboxyl group, the peptide [I] of the present invention could not be successfully dissolved."

Further analysis, however, shows that this statement is nebulous, unsubstantiated, and even if true, would not be effective to undermine the validity of this rejection. First, consider the issue of the LA/GA copolymer that has a terminal carboxyl group, versus the LA/GA copolymer that has no terminal carboxyl group. The following is stated on page 15, line 14+:

> By way of illustration, taking a polymer having a terminal carboxyl group as synthesized from one or more *alpha*-hydroxy acids by the non-catalytic dehydrative poly-condensation process as an example, the number average molecular weight by end-group determination is approximately equal to the number average molecular weight found by GPC. In contrast, in the case of a polymer substantially not containing free terminal carboxyl groups as synthesized from a cyclic dimer by the ring-opening polymerization process and using catalysts, the number average molecular weight by end-group determination is by far greater than the number average molecular weight by GPC determination. By this difference, a polymer having a terminal carboxyl group can be clearly discriminated from a polymer having no terminal carboxyl group. Thus, the term "biodegradable polymer having a terminal carboxyl group" is used herein to mean a biodegradable polymer showing a substantial agreement between the number average molecular weight by GPC determination and the number average molecular weight by end-group determination.

Consider in particular the following passage: "synthesized from a cyclic dimer by the ring-opening polymerization process and using catalysts". It is never made clear in the specification what is meant by this. Which dimer, which catalyst, and what reaction conditions? That is, if a chemist wanted to synthesize a LA/GA copolymer that has no terminal carboxyl group, how would he go about it, and more importantly, what structure would applicants envisage in which the terminal carboxyl group has been eliminated? Applicants may be inclined to argue that the answer to these questions is not necessary in order for one to make and use the claimed invention (or at least some of the embodiments within the claimed invention). However, if applicants are attempting to argue some sort of "unexpected results", these questions do indeed become relevant. At no point in the specification do applicants reveal the structure of the LA/GA copolymer that lacks a terminal carboxyl group. Nor do applicants provide any sort of speculation as to a

possibility for a functional group that might be present at the termini (such that a free carboxyl group is not present). Nor do applicants provide any clues as to how a chemist could synthesize a copolymer from lactic acid and glycolic acid, in the absence of all other reactants, such that a carboxyl group is not present. Of course, one could take a LA/GA copolymer that bears a carboxyl group and esterify or amidate the C-terminal carboxyl group by any of a number of procedures. But if applicants are attempting to imply that it is even possible to synthesize LA/GA copolymer that lacks a terminal carboxyl group just be reacting lactic acid and glycolic acid, in the absence of all other reactants and oxidants, such a proposal would be found to be unpersuasive. Further, there is nothing in the instant specification, or even in applicants arguments that would suggest that the LA/GA copolymer of Boswell lacks a terminal carboxyl group.

In addition to the foregoing, applicants have provided no "unexpected results". There is no side-by-side comparison, and applicants have provided no clues as to the nature of the copolymer which they have prepared such that the terminal carboxyl groups have been eliminated. And even if, at some point in the future, applicants are willing to reveal the conditions under which they obtained the copolymer which lacks the terminal carboxyl group, or the functional groups which they believe to be present at the termini of the copolymer, the fact is that the claims are drawn to a composition, not to a method of dissolving a peptide (as referred to at page 58, line 31+).

The rejection is maintained.

✧

Claims 1-3 and 11-15 are rejected under 35 U.S.C. §103 as being unpatentable over Haviv (USP 5,140,009) in view of Boswell (USP 3,773,919).

Haviv discloses various peptides falling within the scope of instant claim 1. Also disclosed (col 27, line 8+) is that the peptide can be combined with a LA/GA copolymer. Further discussion of the PLA/PLG copolymer is provided in Boswell. Boswell does not disclose any of the LH-RH antagonists to which the instant claims are drawn.

Applicants have argued that they believe that a chemist preparing the LA/GA copolymer of Boswell could not help but convert the terminal carboxyl groups into some other functional group. However, applicants have provided no reason why a skilled chemist would believe such a proposal.

The rejection is maintained.

✧

With regard to JP 63-218632, no abstract has been received. It is suggested that applicants do both of the following: (a) provide an abstract of JP 63-218632, and (b) provide an IDS which lists not the Japanese patent itself, but rather the abstract of the Japanese patent.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800